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Fe-pillared bentonite—an efficient catalyst for sulfonylation of arenes using aryl and alkyl sulfonyl chlorides

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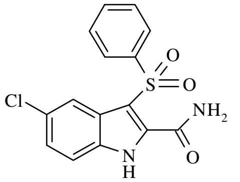
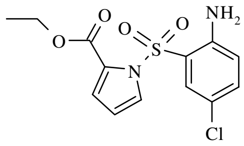
Abstract—Fe-pillared bentonite (Fe-PILC) was shown to be an extremely efficient catalyst for the sulfonylation of activated as well as unactivated carbocyclic aromatic compounds and heterocyclic aromatic compounds. The catalyst was also found to be recyclable.

Aryl sulfones and sulfoxides are interesting functional groups possessing manifold reactivity for conversion to a variety of organosulfur compounds in the field of drugs and pharmaceuticals.[1] In particular, aryl sulfones have received much attention as powerful anti-HIV-1 agents.[2] Indol-3-yl and pyrrolyl aryl sulfones were found to be highly potent and structurally novel non-nucleoside reverse transcriptase inhibitors (NNTRIs), for example, L-737, 126, and PAS.[3,4]



L-737, 126



PAS

The common methods for preparing these sulfones include the oxidation of sulfides[5] or sulfonylation of arenes using an aryl sulfonyl halide or an aryl sulfonic acid in the presence of a strong acid catalyst.[6] Although these methods are attractive, inherent disadvantages encountered in the use of conventional soluble acid catalysts are the generation of large amounts of effluent, the inability to recycle reagents, highly corrosive conditions, and the low selectivity for *para*/*ortho* sulfonylated isomers. They are also incompatible with numerous functional groups including olefins, amines, and some nitrogen heterocycles. Very recently, efficient catalytic protocols have emerged including the use of Fe(III) exchanged montmorillonite clay,[7a] zeolites,[7b] and microwaves in the presence of $FeCl_3$ as catalysts.[7c] However, these reactions often require prolonged heating, a large amount of a sometimes expensive catalyst and fail with unactivated substrates. For the sulfonylation of unactivated aromatics and indoles the most effective reported catalysts are bismuth(III) triflate,[8a,b] indium(III) triflate,[8c] sodium perchlorate,[8d] and $InBr_3$[8e] but these catalysts are very expensive and are not commercially available.

We have recently reported the high activity of Fe-exchanged montmorillonite clays for the acylation of sulfonamides,[9a] the Friedel–Crafts benzylation of arenes with benzyl chlorides,[9b,c,d] the Beckmann rearrangement,[9e] and nitrile formation.[9f] In the present work, we demonstrate that Fe-pillared bentonite (Fe-PILC) functions as an efficient catalyst for the sulfonylation of activated as well as unactivated carbocyclic aromatic compounds and heterocyclic aromatic compounds (Scheme 1).

$$\mathrm{Ar{-}H} + \mathrm{R{-}SO_2Cl} \xrightarrow[\triangle]{\text{Fe - PILC}} \mathrm{Ar{-}SO_2R}$$

$R = CH_3, C_6H_5, p\text{-}CH_3C_6H_4$

Scheme 1. Sulfonylation of arenes using aryl and alkyl sulfonyl chlorides.

Keywords: Fe-pillared bentonite; Sulfonylation; Sulfones.

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The catalyst was prepared by treating bentonite clay with polyoxocations of Fe in an aqueous solution as described earlier.[10] The reaction of *m*-xylene with *p*-toluenesulfonyl chloride was selected as a model to test the activity of different Fe-based catalysts viz. Fe-PILC, K10-FeO,[9b] K10-FeA,[9b] and K10-FePLS[9d] at 120 °C (Table 1). It was found that the Fe-PILC catalyst was superior to all other Fe-based catalysts and gave good yields of product in a short reaction time (15 min) whereas the other catalysts took longer and the yields of the products were less. The Fe^{3+}-K10 (Fe-exchanged montmorillonite)[7a] (Table 1, entry 5) took 6 h for completion of the reaction. The high activity of Fe-PILC may be attributed to the presence of a high content of Fe^{3+}, that is, 20.6%.

Table 1. Sulfonylation of *m*-xylene with *p*-toluenesulfonyl chloride using different Fe-based catalysts at 120 °C

Entry	Catalyst	Fe (%)	Time (h)	Yield (%)[a]
1	Fe-PILC	20.6	0.25	88
2	K10-FeO	3.6	7.0	No reaction
3	K10-FeA	1.12	7.0	No reaction
4	K10-FePLS	4.8	7.0	22
5	Fe^{3+}-K10[b]	6.32	6.0	85

[a] Isolated yield.

[b] As reported in Ref. 7a.

To extend the scope of the reaction and to generalize the procedure, we investigated the reactions of a series of aromatic hydrocarbons with a variety of sulfonyl chlorides viz. *p*-toluenesulfonyl chloride, benzenesulfonyl chloride, and methanesulfonyl chloride, in the presence of Fe-PILC as catalyst at different temperatures to obtain the corresponding sulfones (Table 2).[11] Fe-PILC is capable of catalyzing not only the sulfonylation of activated arenes but also non- or weakly-activated ones. In the synthesis of diphenyl sulfone (Table 2, entry j), an intermediate for the synthesis of Dapsone (4,4-diaminophenyl sulfone),[12] which is effective for leprosy

Table 2. Fe-PILC-catalyzed sulfonylation of arenes with aryl and alkyl sulfonyl chlorides[a]

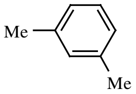
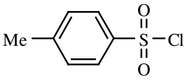
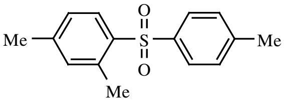
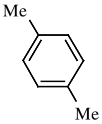
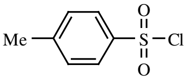
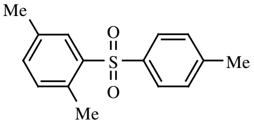
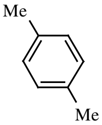
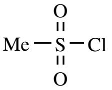
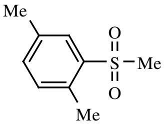
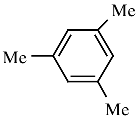
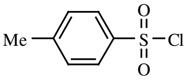
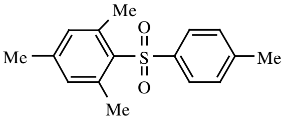
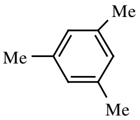
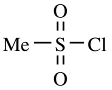
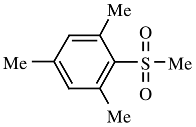
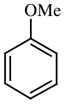
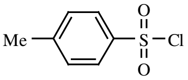
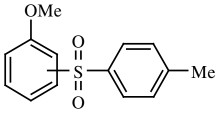
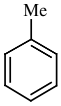
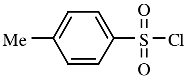
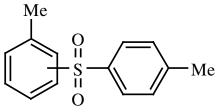
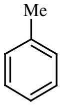
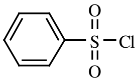
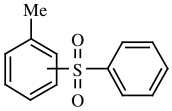
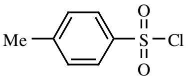
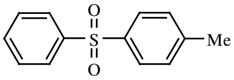
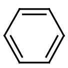
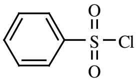
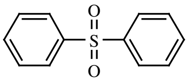
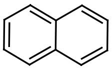
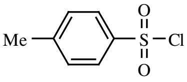
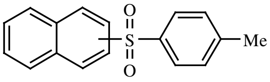
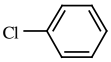
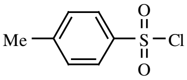
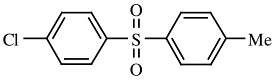
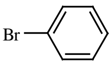
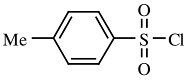
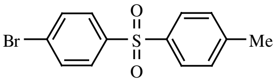
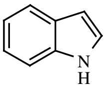
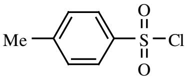
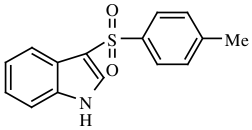
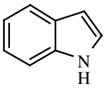
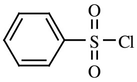
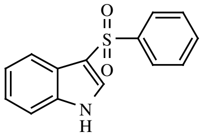
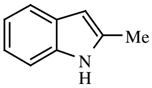
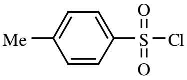
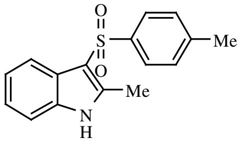
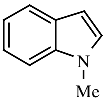
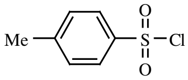
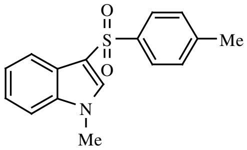
Entry	Arene **1**	Sulfonyl chloride **2**	Sulfone **3**	Reaction conditions time/temperature	Yield (%)[b] [*o*:*m*:*p*]
a				15 min/120 °C	88
b				15 min/120 °C	84
c				45 min/120 °C	76
d				10 min/120 °C	92
e				45 min/120 °C	78
f				10 min/120 °C	84 [35.2:0:64.8]
g				2 h/110 °C	80 [38.9:0:61.1]
h				2 h/110 °C	74 [41.4:0:58.6]
i				8 h/80 °C	72

Table 2 (*continued*)

Entry	Arene **1**	Sulfonyl chloride **2**	Sulfone **3**	Reaction conditions time/temperature	Yield (%)[b] [*o*:*m*:*p*]
j				8.5 h/80 °C	70
k				20 min/120 °C	88 [63.2:36.8][c]
l				12 h/120 °C	74
m				12 h/120 °C	71
n				7 h/80 °C	88
o				8 h/80 °C	83
p				6.5 h/80 °C	92
q				9 h/80 °C	63

[a] Arene: 5 mL; sulfonyl chloride: 3 mmol; Fe-PILC: 0.2 g.

[b] Isolated and unoptimized yield.

[c] Isomers distribution based on ^{1}H NMR, α:β = 63.2:36.8.

treatment, the use of the solid acid (Fe-PILC) offers a commercially feasible route with control of solid effluents. Noteworthy results were also observed for the sulfonylation of deactivated chloro- and bromobenzenes (Table 2, entries l and m) and indole derivatives (Table 2, entries n–q). A variety of indoles reacted smoothly with sulfonyl chlorides in dichloroethane at reflux with high regioselectivity. No *N*-substituted products were observed under these reaction conditions. This is probably due to the stabilization of the imine–enamine complex by the Lewis acid during sulfonylation.[8e] An activated indole gave the sulfonylated product in excellent yield (Table 2, entry p). Treatment of the *N*-protected indole, *N*-methylindole with *p*-toluenesulfonyl chloride in dichloromethane at 80 °C for 9 h also afforded the corresponding sulfone in 63% yield. Furan and pyrrole were found to be unreactive under identical conditions.

The recyclability of the catalyst, was also studied. After each cycle the catalyst was filtered and activated at 80 °C before using for the next cycle. The activity of the catalyst was unaffected even after three cycles.

In summary, Fe-PILC has been found to be a novel inexpensive and highly efficient catalyst for sulfonylation of activated as well as unactivated carbocyclic aromatic compounds and heterocyclic aromatic compounds.

Acknowledgements

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10. Fe-pillared bentonite clay (Fe-PILC) was prepared as reported in Rightor, E. G.; Tzou, M. S.; Pinnavaia, T. J. *J. Catal.* **1991**, *130*, 29–40.
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